Pain Management In Lung Cancer

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Introduction

• Lung cancer is the most common cancer in the world with 1.61 million new cases diagnosed every year.

• The majority of patients with lung cancer have an advanced stage of the disease at clinical presentation.

• Pain is the most common symptom in cancer patients in general as it also is for lung cancer specifically.

• Patients with lung cancer experience more symptom distress than patients with other types of cancers.
Impact of pain

- Symptoms such as pain may be associated with worsening of other symptoms (physically and emotionally).
- Function.
- Socially.
- Affect the quality of life.
Type of pain

Pathophysiologial

Somatic (80%)
* Superficial
* Aching
* Well localized

Visceral (30%)
* Dull
* Deep
* Poorly localized

Neuropathic (40%)
* Sharp
* Burning
* Electrical
## Causes of lung cancer pain – tumor related

<table>
<thead>
<tr>
<th>Intra-thoracic</th>
<th>Extra-thoracic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pleural invasion</td>
<td>• Metastasis:</td>
</tr>
<tr>
<td>• Chest wall invasion</td>
<td>o Bone</td>
</tr>
<tr>
<td>• Obstructive pneumonitis</td>
<td>o Liver</td>
</tr>
<tr>
<td>• Pulmonary embolus</td>
<td>o Brain</td>
</tr>
<tr>
<td>• Costopleural syndrome</td>
<td></td>
</tr>
<tr>
<td>• Tumor invasion</td>
<td>• Hypertrophic osteo-arthropathy</td>
</tr>
<tr>
<td>(malignant brachial plexopathy)</td>
<td>• Pathological fractures</td>
</tr>
</tbody>
</table>
## Treatment Induced Pain

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Radiation Therapy</th>
<th>Surgical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vinca alkaloid</td>
<td>• Duo to direct toxic effect or microinfarction of nerves.</td>
<td>• Thoracotomy</td>
</tr>
<tr>
<td>• Cisplatinum</td>
<td>• Pain severity depends on dose and fraction size</td>
<td>• Lobectomy</td>
</tr>
<tr>
<td>• Placlitaxel</td>
<td>• E.g. Brachial plexopathy, esophagitis</td>
<td>• Pneumonectomy</td>
</tr>
<tr>
<td>*distal painful paresthesias and sensory loss during and after treatment.</td>
<td></td>
<td>• Thoracocentesis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use of chest tubes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Biopsy</td>
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</tbody>
</table>
Causes of pain in advanced lung cancer

The three main causes of pain in patients with advanced lung cancer are skeletal metastatic disease (34%), pancoast tumor (31%), and chest wall disease (21%).
Principles of Pain management

Good pain management starts with good pain assessment

**Detailed history**
- Pain description
- Associated symptoms
- Psychosocial history
- Medication/ side effects
- Impact of pain
- Goals of care

**Physical Examination**
- Sings surgical scars
- Swellings
- Tenderness
- Function
- Neurological signs

**Investigations**
- Imaging studies
- RFT
- LFT
- CBC
Principles of Pain Management

1. Non-opioid analgesics
   - Aspirin
   - Acetaminophen
   - NSAIDs

2. “Weak” opioid analgesics
   - Codeine
   - Hydrocodone
   - Oxycodone

3. “Strong” opioid analgesics
   - Morphine
   - Hydromorphone
   - Oxycodone
   - Methadone
# Pharmacotherapy

<table>
<thead>
<tr>
<th>Weak analgesics</th>
<th>Strong analgesics</th>
<th>Co-analgesics</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Paracetamol</td>
<td>• Opioids</td>
<td>• Antidepressants:</td>
</tr>
<tr>
<td>• NSAIDs</td>
<td>o Morphine</td>
<td>o TCA (amitriptyline/nortriptyline)</td>
</tr>
<tr>
<td>• Aspirin</td>
<td>o Hydromorphone</td>
<td>o SNRI(venlafaxine)</td>
</tr>
<tr>
<td>• Topical analgesics</td>
<td>o Oxycodone / oxycontin</td>
<td>• Anticonvulsant:</td>
</tr>
<tr>
<td>• Codeine</td>
<td>o Fentanyl</td>
<td>o Gabapentin</td>
</tr>
<tr>
<td>• tramadol</td>
<td>o Sufentanil</td>
<td>o Pregabalin</td>
</tr>
</tbody>
</table>

### Opioids
- Morphine
- Hydromorphone
- Oxycodone / oxycontin
- Fentanyl
- Sufentanil
- Methadone

### Antidepressants:
- TCA (amitriptyline/nortriptyline)
- SNRI (venlafaxine)

### Anticonvulsant:
- Gabapentin
- Pregabalin

### NMDA antagonists:
- Ketamine

### Na channel blockers:
- Lidocaine
- Capsaicin

### Corticosteroids
Opioids and concern about survival

Opioid Use amongst Cancer Patients at the End of Life

Lalit Kumar Radha Krishna,1 MBBS, MRCP(UK), Jissy Vijo Poulose,2 MBBS, MMed (Public Health), Benjamin SA Tan,1 MBBS, Cynthia Goh,1,2 MBBS, PhD, FAMS

[Graphs showing cumulative survival with opioids 24 hours before death and dose categories with survival days and p-values.]
Time to maximal plasma concentration - opioids

- IV dosing = 6 minutes
- SC/IM dosing = 30 min
- po/pr dosing = 60 min
Principles of opioid use in cancer pain

**Cancer pain**

**Intermittent**
- Mild to moderate
- Needs BT (PRN) dose
- < 4 times/day

**Persistent**
- Moderate to severe
- Needs regular dose (around the clock) + BT dose
Breakthrough cancer pain

Gradual
- Gradual onset (30 min)
- Lasts longer than 1 h
- IR opioids are enough (PO/SC/IV)

Rapid (Incident pain)
- Rapid onset (5 – 10 min)
- Short duration (<1h)
- Rapid acting opioid (Sufentanil, intranasal fentanyl)
Constant (persistent) cancer pain
Causes of breakthrough pain

- End of dose failure
- Incident pain (movement induced)
- Idiopathic pain (Spontaneous)
End of dose failure

Pain intensity

Side effects
Incident pain
Frequency and safety of opioids

- Regular dose every 4 hours with normal renal and liver function.
- Given every 6 hours in renal or liver impairment.
- Fentanyl and methadone are the safest in renal impairment.
- Fentanyl is safe in liver impairment but methadone is not.
- Breakthrough dose usually given Q1 hour = 10% of total daily dose.
- Opioids should be held if:
  - RR<10 or patient over sedated
  - BP is very low
How to start opioids?

It depends on:

- Patient age
- Co morbidity
- Renal and liver functions
- Opioid naïve or not
- Patient’s Previous experience with side effects and tolerability
- Pain severity
- Patient’s general condition
Opioid Naïve Patient

INITIATING SHORT-ACTING OPIOIDS IN OPIOID-NAÏVE PATIENTS

Monitor for acute and chronic adverse effects. (See Management of Opioid Adverse Effects PAIN-5)

Opioid-Naïve Patients

Initial Dose

- Oral (peak effect 60 min)
  - Dose 5-15 mg oral short-acting morphine sulfate or equivalent (See PAIN-6)
  - Reassess efficacy and adverse effects at 60 min

- Intravenous bolus (peak effect 15 min) or patient-controlled analgesia (PCA)
  - Dose 2-5 mg intravenous morphine sulfate or equivalent (See PAIN-6)
  - Reassess efficacy and adverse effects at 15 min

Subsequent Dose

- Pain score unchanged or increased
  - Increase dose by 50%-100%
  - Repeat same dose

- Pain score decreased to 0-3
  - Continue at current effective dose as needed over initial 24 h

- Pain score decreased to 4-6
  - Increase dose by 50%-100%
  - Repeat same dose

After 2-3 cycles, consider IV titration and/or see PAIN-5 for subsequent management and treatment

See Subsequent Pain Management, Mild Pain 0-3 (PAIN-6)
Opioid tolerant patient
Management of Opioid side effects

• **Constipation** (stimulant + osmotic laxatives) for all patients on opioids.
• **Nausea and vomiting** (metoclopramide +/- other antiemetic).
• **Sedation** (hydration, reduce the dose or rotate to other drug + reassurance of family)
• **Respiratory depression** (hold + naloxone + rotate to other drug).
• **hallucination** (hydration + haloperidol + reduce dose or rotate to other drug).
• **Urinary retention** (catheterization + hydration + rotation)
• **Neurotoxicity** (hyperalgesia and allodynia) reduce or rotate + Haldol + clonazepam
After the pain is controlled

- Switch to long acting formula:
  - Morphine SR
  - Oxycontin
  - Tramadol SR
  - Hydromorphone SR
  - Fentanyl patch (TD Q72hs)

- Keep IR opioid additional to Q1h PRN for episodic pain.
Short acting vs. long acting opioid
## Neuropathic pain pharmacotherapy

<table>
<thead>
<tr>
<th>Anticonvulsants</th>
<th>TCA</th>
<th>NMDA antagonists</th>
<th>Na channel blockers</th>
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</thead>
<tbody>
<tr>
<td><strong>Pregabalin</strong> (75 – 300 mg)</td>
<td><strong>Amitriptyline</strong> (10mg ..)</td>
<td><strong>Ketamine infusion</strong></td>
<td><strong>Lidocaine</strong></td>
</tr>
<tr>
<td><strong>Gabapentin</strong> (100 – 3600mg)</td>
<td><strong>Nortriptyline</strong> (25mg ..)</td>
<td><strong>Side effects: dizziness , drowsiness , hallucination.</strong></td>
<td>o Patch</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Midazolam should be added to control symptoms</strong></td>
<td>o gel</td>
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<tr>
<td></td>
<td></td>
<td><strong>At rate 5mg/h</strong></td>
<td><strong>Capsaicin</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Increased daily</strong></td>
<td>o Patch</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>For few days only and stop</strong></td>
<td>o gel</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Side effects: constipation, postural hypotension, urinary retention.</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Should be avoided in cardiac patients</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Should be adjusted in renal failure.</strong></td>
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Corticosteroids

• Dexamethasone has less mineralocorticoid effect.
• Reduce edema around tumor and reduce tumor size.
• Help to ease the pain and nausea.
• Patient should be on PPI to protect the stomach.
• Watch carefully BP and blood sugar.
• Starting from 2mg – 16 mg daily.
• When you decide to stop taper off gradually unless within 2 weeks.
Interventional procedures

- Intercostal nerve block
- Epidural or intrathecal neuroaxial block
- Rhizotomy (surgical or chemical neurolysis)
- Percutaneous cementoplasty
Bone metastasis

- 20% with NSCLC and 40% with SCLC.
- Periosteal inflammation and elevation and destruction of the primary afferents within bones are the most common mechanisms of pain from bone metastases.
- The gold standard treatment for pain due to bone metastases is radiotherapy (single fraction).
- If a metastasis occurs in a weight bearing bone, prophylactic surgical stabilization should be considered before a pathological fracture occurs.
- Post-operative radiotherapy is recommended regardless of the type of surgical procedure chosen for bony metastases.
- Bisphosphonates have assumed an important role in the treatment of patients with bone metastasis.
Brain metastasis

- 30% with NSCLC and 50% with SCLC after 2 years of diagnosis.
- Pain is associated with brain edema and increased pressure.
- Could be treated with:
  - Dexamethasone
  - surgical resection
  - radiation therapy
  - chemotherapy
Additional approaches

• Psychological support.
• Relaxation techniques.
• Breathing exercise.
• Acupuncture.
• TENS.
Thank You
Questions?
Management of Lung Cancer Pain

Case Presentation
Case (1)

• 52 year old lady with history of non small cell carcinoma right lung diagnosed 6 months ago. treated with surgery and chemotherapy. Complaining of right sided chest wall pain severe enough to interrupt her sleep.

• What are you thinking of ?
history

- Severe pain 15/10 started since 2 months
- Sharp electrical pain burning sometimes
- Radiating to back
- Increasing gradually with time
- Not relieved by Tramadol, Prufen and Paracetamol
- Unable to sleep or do his daily activities
O/E

- Site: around the surgical scar which looks clean
- No tenderness
- Feels some numbness and tingling sensations around the scar
- Neurological dermatomal examinations showed decreased sensation over the affected area.
Imaging studies

- CXR, CT scan, bone scan showed no progression of disease
- No evidence of bone metastasis
Diagnosis?

Post Thoracotomy Pain Syndrome
Post Thoracotomy Pain Syndrome

• Definition – IASP 1982
  pain that recurs or persists along a thoracotomy scar more than 2 months after surgery.
• Incidence – 30 to 50 % (>30 % at 3 years)
• post thoracotomy pain that persists after 6 weeks usually becomes chronic
Mechanisms and risk factors

1) injury to intercostal nerves
   (pain signals from chest wall costal pleura)

• Factors:
  o Surgical incision
  o Rib retraction
  o Chest tube placement
  o Suturing technique (pericostal suture injury)
  o Rib fractures
mechanisms

• 2) Injury to Costochondral cartilage
• 3) Ipsilateral shoulder pain – can relate to muscle trauma
   (latissimus dorsi or serratus anterior) → adhesive capsulitis
Management - Chronic

- r/o tumor recurrence
- NSAIDs / Cox 2
- Opioids
- TCA
- Ca channel blockers / antiepileptics (pregabalin, gabapentin)
- SNRI (duloxetine, minicilpran, venlafaxine)
- Ketamine
- Lidocaine patches
- Botulinum toxin
- TENS
case (2)

• 60 year old man with history of small cell lung cancer diagnosed recently with advanced non operable disease refused to take any chemotherapy. Complaining of severe back pain associated with LT leg pain.

• How to manage his pain?
history

- aching, sometimes sharp electrical
- 8/10
- Increased with movement or sitting
- Radiate to left lower limb
- Associated with numbness over left leg
- Decreased little bitt with Tylenol 3 but not satisfied with pain control
- Using Paracetamol regular every 6 hs + Celebrex (NSAID)
O/E

• Lying on the bed
• Looks in severe pain
• Local examination: tenderness over lower part of the back but no swelling
• Both lower limbs not swollen
• Neurological examination: decreased power and sensation in the left side compared to right side
investigation

• MRI showed spinal cord compression at L4-L5, L5-S1.
Treatment

- Dexamethasone 16mg iv daily.
- Urgent consultation:
  - Neurosurgery
  - Radiation oncology
- Control pain:
  - morphine CIVI (titrated up to 10mg/hr)
  - Pregabalin 75mg po bid
  - Amitriptyline 10mg po qhs
Questions?